

**IN THE UNITED STATES DISTRICT COURT  
FOR THE DISTRICT OF DELAWARE**

MEDPOINTE HEALTHCARE INC.,  
Plaintiff,

vs.

APOTEX INC. and APOTEX CORP.,  
Defendants.

C. A. No. 07-204-SLR

## PLAINTIFF'S REPLY TO DEFENDANTS' COUNTERCLAIMS

Plaintiff MedPointe Healthcare Inc. ("MedPointe"), for its Reply to the counterclaims of Defendants Apotex Inc. and Apotex Corp. (collectively, "Apotex"), hereby states as follows:

**COUNTERCLAIM PARAGRAPH 1**

Apotex, Inc. is a Canadian corporation having a place of business at 380 Elgin Mills Road East, Richmond Hill, Ontario, Canada L4C 5H2.

**REPLY TO COUNTERCLAIM PARAGRAPH 1**

Upon information and belief, MedPointe admits that Apotex Inc. is a Canadian corporation having a place of business at 380 Elgin Mills Road East, Richmond Hill, Ontario, Canada L4C 5H2.

**COUNTERCLAIM PARAGRAPH 2**

Apotex Corp. is a Delaware corporation having a place of business at 2400 North Commerce Parkway, Suite 400, Weston, Florida 33326.

**REPLY TO COUNTERCLAIM PARAGRAPH 2**

Upon information and belief, MedPointe admits that Apotex Corp. is a Delaware corporation having a place of business at 2400 North Commerce Parkway, Suite 400, Weston, Florida 33326.

**COUNTERCLAIM PARAGRAPH 3**

MedPointe Healthcare Inc. ("MedPointe") is a Delaware corporation having a place of business at 265 Davidson Avenue, Somerset, New Jersey 08873.

**REPLY TO COUNTERCLAIM PARAGRAPH 3**

Admitted.

**COUNTERCLAIM PARAGRAPH 4**

MedPointe purports to be the sole owner of United States Patent No. 5,164,194 ("the '194 patent"), entitled "AzelaStine Containing Medicaments."

**REPLY TO COUNTERCLAIM PARAGRAPH 4**

MedPointe admits that since August 16, 2002, MedPointe has been, and continues to be, the sole owner of the '194 patent. To the extent that Counterclaim Paragraph 4 contains any other or different averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 5**

Apotex Inc. has submitted an Abbreviated New Drug Application ("ANDA") 78-621 for a proposed drug product containing azelastine hydrochloride for ocular administration.

**REPLY TO COUNTERCLAIM PARAGRAPH 5**

Upon information and belief, MedPointe admits that on or about December 13, 2006, Apotex submitted ANDA 78-621 to the FDA under § 505(j) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 355(j)). Upon information and belief, MedPointe admits that ANDA 78-621 seeks the FDA approval necessary to engage in the commercial manufacture, use, offer for sale and sale of a generic ophthalmic solution product containing 0.05% azelastine hydrochloride. To the extent that Counterclaim Paragraph 5 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 6**

Pursuant to 21 U.S.C. § 355 (j)(2)(A)(vii) and 21 C.F.R. § 314.95, Apotex Inc. certified to MedPointe that the '194 patent is invalid, unenforceable, and/or will not be infringed by the manufacture, use, or sale of the proposed drug for which ANDA 78-621 is submitted.

**REPLY TO COUNTERCLAIM PARAGRAPH 6**

Upon information and belief, MedPointe admits that ANDA 78-621 contains an allegation under § 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 355(j)(2)(A)(vii)(IV)) that the claims of the '194 patent are either invalid, unenforceable and/or

will not be infringed by the manufacture, use or sale of the generic drug product for which ANDA 78-621 was submitted. MedPointe further admits that, as required by 21 C.F.R. § 314.95, Apotex provided MedPointe with written notification of ANDA 78-621 and its § 505(j)(2)(A)(vii)(IV) allegation. To the extent that Counterclaim Paragraph 6 contains any other or additional averments, MedPointe denies them.

#### **COUNTERCLAIM PARAGRAPH 7**

MedPointe has commenced this civil action against Apotex Inc. and Apotex Corp. alleging patent infringement.

#### **REPLY TO COUNTERCLAIM PARAGRAPH 7**

MedPointe admits that it commenced this action against Apotex Inc. and Apotex Corp. and that its Complaint alleges infringement of the '194 patent. To the extent that Counterclaim Paragraph 7 contains any other or additional averments, MedPointe denies them.

#### **COUNTERCLAIM PARAGRAPH 8**

This case arises under the Constitution, laws, or treaties of the United States, viz., 35 U.S.C. §§ 1-376, which is an Act of Congress relating to patents, and 21 U.S.C. § 355, which provide subject matter jurisdiction under 28 U.S.C. §§ 1331 and 1338(a) and 35 U.S.C. § 271(e)(5).

#### **REPLY TO COUNTERCLAIM PARAGRAPH 8**

MedPointe admits that Apotex purports to state declaratory judgment counterclaims that arise under 28 U.S.C. §§ 2201 and 2202 and the Patent Laws of the United States, 35 U.S.C. § 1, *et seq.* MedPointe further admits that this Court has subject matter jurisdiction over these counterclaims pursuant to 28 U.S.C. §§ 1331 and 1338(a). MedPointe, however, denies that there is any factual or legal basis for these counterclaims. To the extent that Counterclaim Paragraph 8 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 9**

Venue and personal jurisdiction are proper in this district because MedPointe, *inter alia*, is subject to personal jurisdiction in this judicial district and has submitted itself to the jurisdiction of this court.

**REPLY TO COUNTERCLAIM PARAGRAPH 9**

Admitted.

**COUNTERCLAIM PARAGRAPH 10**

A real, actual, and justiciable controversy exists between Apotex Inc. and Apotex Corp. on the one hand and MedPointe on the other hand regarding the invalidity of the '194 patent and Apotex's non-infringement thereof, constituting a case of actual controversy within the jurisdiction of this Court under the Declaratory Judgment Act, 28 U.S.C. §§ 2201-2202 (2005).

**REPLY TO COUNTERCLAIM PARAGRAPH 10**

MedPointe admits that Apotex, by infringing the '194 patent, has created an actual and justiciable controversy between itself and MedPointe regarding that infringement. MedPointe further admits that Apotex purports to state declaratory judgment counterclaims that arise under 28 U.S.C. §§ 2201 and 2202 and the Patent Laws of the United States, 35 U.S.C. § 1, *et seq.* MedPointe, however, denies that there is any factual or legal basis for these counterclaims. To the extent that Counterclaim Paragraph 10 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 11**

Apotex Inc. and Apotex Corp. repeat, reallege and incorporate by reference each of the allegations of paragraphs 1 through 10 as though set forth fully herein.

**REPLY TO COUNTERCLAIM PARAGRAPH 11**

MedPointe restates its responses to Counterclaim Paragraphs 1 through 10 as though fully set forth herein. To the extent that Counterclaim Paragraph 11 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 12**

The '194 patent is invalid and/or unenforceable on grounds specified in United States Code, Title 35, including failure to comply with one or more of the requirements of 35 U.S.C. §§ 101, 102, 103, and/or 112.

**REPLY TO COUNTERCLAIM PARAGRAPH 12**

Denied.

**COUNTERCLAIM PARAGRAPH 13**

Apotex Inc. and Apotex Corp. repeat, reallege and incorporate by reference each of the allegations of paragraphs 1 through 12 as though set forth fully herein.

**REPLY TO COUNTERCLAIM PARAGRAPH 13**

MedPointe restates its responses to Counterclaim Paragraphs 1 through 12 as though fully set forth herein. To the extent that Counterclaim Paragraph 13 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 14**

The '194 patent issued November 17, 1992 from patent application number 07/551,644 filed July 12, 1990, which purported to be a continuation of patent application number 07/268,772, filed November 9, 1988, and subsequently abandoned, which purported to claim priority from German patent application number 3738681, filed November 13, 1987.

**REPLY TO COUNTERCLAIM PARAGRAPH 14**

MedPointe admits that the '194 patent issued on November 17, 1992 from U.S. patent application serial number 07/551,644 ("the '644 application") filed on July 12, 1990, which was a continuation of U.S. patent application serial number 07/268,772 filed on November 9, 1988 and subsequently abandoned, and claims priority from German patent application number 3738681 filed on November 13, 1987. To the extent that Counterclaim Paragraph 14 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 15**

United States Patent No. 3,813,384 ("the '384 prior art patent") is prior art with regard to the '194 patent under one or more of the provisions of 35 U.S.C. § 102.

**REPLY TO COUNTERCLAIM PARAGRAPH 15**

MedPointe admits that United States Patent No. 3,813,384 bears on its face an issue date that is prior to the filing date of the earliest application to which the '194 patent claims priority, German patent application number 3738681 filed on November 13, 1987. To the extent that Counterclaim Paragraph 15 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 16**

United States Patent No. 4,704,387 ("the '387 prior art patent") is prior art with regard to the '194 patent under one or more of the provisions of 35 U.S.C. § 102.

**REPLY TO COUNTERCLAIM PARAGRAPH 16**

MedPointe admits that United States Patent No. 4,704,387 bears on its face an issue date that is prior to the filing date of the earliest application to which the '194 patent claims priority, German patent application number 3738681 filed on November 13, 1987. To the extent

that Counterclaim Paragraph 16 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 17**

The '194 patent is invalid under 35 U.S.C. § 102 over prior art including, for example, the '384 and '387 patents.

**REPLY TO COUNTERCLAIM PARAGRAPH 17**

Denied.

**COUNTERCLAIM PARAGRAPH 18**

Apotex Inc. and Apotex Corp. repeat, reallege and incorporate by reference each of the allegations of paragraphs 1 through 17 as though set forth fully herein.

**REPLY TO COUNTERCLAIM PARAGRAPH 18**

MedPointe restates its responses to Counterclaim Paragraphs 1 through 17 as though fully set forth herein. To the extent that Counterclaim Paragraph 18 contains any other or additional averments, MedPointe denies them.



**COUNTERCLAIM PARAGRAPH 19**

The scope and content of the prior art includes, but is not limited to, United States Patent Nos. 3,813,384; 4,704,387; 3,878,217; 4,254,129; 4,313,931; 4,430,343; Pecoud, A., et al., *International Archives of Allergy and Applied Immunology* (1987), Vol. 82, pp. 541-543; Feinberg, S. M., *Transactions American Academy of Ophthalmology and Otolaryngology* (1950), Vol. 124, pp. 284-286; Kirkegaard, J., et al., *British Journal of Diseases of the Chest* (1983), Vol. 77, pp. 113-122; Pipkorn, U., et al., *Allergy* (1985), Vol. 40, pp. 491-496; Vanden Bussche, G., *Drugs of the Future* (1986), Vol. 11, pp. 841-843; Bende, M., et al., *Allergy* (1987), Vol. 42, pp. 512-515; Diamantis W., et al., *Pharmacologist* (1981), Vol. 23, p. 149; Diamantis W., et al., *Pharmacologist* (1982), Vol. 24, p. 200; and Kubo N., et al., *Jpn. J. Pharmacol.* (1987), Vol. 43, pp. 277-282. The '194 patent is obvious in view of these references either individually, in combination with the knowledge of the person having ordinary skill in the art, or in combination with each other.

**REPLY TO COUNTERCLAIM PARAGRAPH 19**

MedPointe admits that United States Patents No. 3,813,384, 4,704,387, 3,878,217, 4,254,129, 4,313,931, 4,430,343 bear on their faces issue dates that are prior to the filing date of the earliest application to which the '194 patent claims priority, German patent application number 3738681 filed on November 13, 1987. MedPointe also admits that Feinberg, S. M., *Transactions American Academy of Ophthalmology and Otolaryngology* (1950), Vol. 124, pp. 284-286; Kirkegaard, J., et al., *British Journal of Diseases of the Chest* (1983), Vol. 77, pp. 113-122; Pipkorn, U., et al., *Allergy* (1985), Vol. 40, pp. 491-496; Vanden Bussche, G., *Drugs of the Future* (1986), Vol. 11, pp. 841-843; Diamantis W., et al., *Pharmacologist* (1981), Vol. 23, p. 149; and Diamantis W., et al., *Pharmacologist* (1982), Vol. 24, p. 200 are dated on their faces before the earliest application to which the '194 patent claims priority. MedPointe further admits that Pecoud, A., et al., *International Archives of Allergy and Applied Immunology* (1987), Vol. 82, pp. 541-543; Bende, M., et al., *Allergy* (1987), Vol. 42, pp. 512-515; and Kubo N., et al., *Jpn J. Pharmacol.* (1987), Vol. 43, pp. 277-282 are dated on their faces in 1987. To the extent that Counterclaim Paragraph 19 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 20**

The differences between the subject matter claimed in the '194 patent and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

**REPLY TO COUNTERCLAIM PARAGRAPH 20**

Denied.

**COUNTERCLAIM PARAGRAPH 21**

Apotex Inc. and Apotex Corp. repeat, reallege and incorporate by reference each of the allegations of paragraphs 1 through 20 as though set forth fully herein.

**REPLY TO COUNTERCLAIM PARAGRAPH 21**

MedPointe restates its responses to Counterclaim Paragraphs 1 through 20 as though fully set forth herein. To the extent that Counterclaim Paragraph 21 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 22**

The '194 patent is unenforceable because it was procured through inequitable conduct. In violation of their duty of candor to the United States Patent & Trademark Office ("PTO"), applicants for the '194 patent misled the PTO about the properties of the alleged invention claimed therein. More particularly, circumstances constituting the applicants' inequitable conduct include, but are not limited to, affirmative misrepresentation regarding the advantages and benefits of azelastine administered to prophylactically treat allergies.

**REPLY TO COUNTERCLAIM PARAGRAPH 22**

Denied.

**COUNTERCLAIM PARAGRAPH 23**

On August 12, 1985, Jurgan Engel and Gerhard Scheffler filed an application in the PTO claiming compounds that were derivatives of azelastine and like azelastine were antiallergic and antiasthma prophylactically active. The applicants argued the compounds were better than azelastine because they could be applied as an aerosol with no, or considerably, less, bitter taste. On February 16, 1987, a declaration was filed in support of patentability of the derivative compounds wherein the declarant asserted the derivatives of azelastine were superior to azelastine because "[azelastine] cannot be applied in the form of an aerosol" and that "use as an aerosol is especially important for antiallergic and asthma prophylactic compounds." The declarant also argued the compounds of Examples 2 and 4 of the application "have almost 3 times as strong an antiallergic and asthma prophylactic action as [azelastine]." The declarant was an employee of Asta-Werke, but failed to disclose this fact to the PTO. The application later issued as the '387 prior art patent.

**REPLY TO COUNTERCLAIM PARAGRAPH 23**

MedPointe admits that Juergen Engel and Gerhard Scheffler are listed as Applicants for U.S. Patent Application No. 764,995 ("the '995 application"), which indicates on its face a filing date of August 12, 1985. MedPointe further admits that the '995 application included claims for "substituted benzylphthalazinone[s]." MedPointe admits that the '995 application stated, *inter alia*:

The compounds of the invention are antiallergic and asthma prophylactically active, however, considerably stronger and better than the known compounds of German patent 2164058. Furthermore, in contrast to the known medicine AZELASTIN (compound according to Example 5 of German patent 2164058) they have either no, or a considerably less, bitter taste, so that they can be applied for example even as an aerosol.

MedPointe admits that the file history of the '995 application includes a declaration dated February 16, 1987 ("the February 16, 1987 Declaration"). MedPointe further admits that the February 16, 1987 Declaration states that "[s]ince 1976, she [the declarant] has been laboratory leader (isolated organ pulmology) in the Pharmaceutical Investigations Division of the Chemiewerke, Homburg." To the extent that Counterclaim Paragraph 23 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 24**

On November 13, 1987, less than nine months from the date the declaration was filed in support of the Engel and Scheffler application, Helmut Hettche filed an application in the Federal Republic of Germany claiming azelastine containing medicaments. The application claimed azelastine medicaments administered as aerosols to prophylactically treat allergy. The application further claimed that azelastine containing medicaments administered as aerosols resulted in no bitter taste side effect. On July 12, 1990, Helmut Hettche filed an application in the United States Patent Office claiming foreign priority to the application filed in the Federal Republic of Germany on November 13, 1987.

**REPLY TO COUNTERCLAIM PARAGRAPH 24**

MedPointe admits that German Patent Application number 373681 was filed on November 13, 1987. MedPointe further admits that the '644 application was filed on July 12, 1990 and claims priority from German patent application number 3748681. MedPointe further admits that Helmut Hettche is the applicant for the '644 application. MedPointe further admits that the '644 application states that:

Furthermore the invention provides a way to overcome problems which arise because of azelastine's exceptionally penetrating, bitter taste. The degree of the bitter taste is so intense that it is even found to be unpleasant in a dilution of 1 : 10<sup>6</sup>. This problem has hitherto prevented oral application of azelastine solutions, since patients refuse to take such azelastine solutions or suspensions. It was surprisingly found in trial subjects that this bitter taste was no longer in evidence when the azelastine formulations of the invention were sprayed into the nose. As a result, it is possible in this manner to apply solutions or suspensions of azelastine and its salts nasally without taste impairment. Moreover the bitter taste is barely perceptible when the sprayed azelastine solution or suspension runs down into the pharynx.

MedPointe is without knowledge or information sufficient to form a belief as to the truth of the remaining averments in Counterclaim Paragraph 24 and therefore denies them.

**COUNTERCLAIM PARAGRAPH 25**

On February 12, 1990, a declaration was filed in support of the '194 patent application and to overcome an obviousness rejection based in part on the '387 prior art patent. The declarant argued azelastine was twice as effective as the compound of Example 1 of the '387 prior art patent. The applicants prosecuting the patent argued these results were surprising and unexpected and supported a finding that the '194 medicaments were not obvious in view of the '387 patent. The applicants failed to inform the examiner that the '387 patent claimed five different compounds and that Example 4 was structurally closer to azelastine and should have been compared to azelastine. The examiner, nonetheless, rejected the declaration anyway because there was an incomplete recitation of the study protocol used to obtain the results.

**REPLY TO COUNTERCLAIM PARAGRAPH 25**

MedPointe admits that the file history of the '644 application includes a declaration dated January 23, 1990 ("the January 23, 1990 Declaration") that appears to have been submitted to the patent office with a letter dated February 12, 1990 stating, *inter alia*, that "the information in the declaration supports the patentability of the claims." MedPointe further admits that the file history of the '644 application includes a request for reconsideration dated December 26, 1989 ("the December 26, 1989 Request for Reconsideration") that discussed "comparative experiment[s]" and stated:

In the case of azelastine, the inhibition was 47.1% whereas, in the case of the compound of Example 1 of the cited Engel patent, the inhibition was only 24.4%.

Thus, azelastine was about twice as effective as the compound of Engel 1 of the Engel patent. This result is surprising and unexpected.

For this reason, it is submitted that the claimed process is unobvious.

MedPointe further admits that the December 26, 1989 Request for Reconsideration stated, *inter alia*:

Engel et al discloses compounds whose structures are similar to that of the presently claimed azelastine, differing in the R group. In the Engel patent, R is benzyl, phenethyl, methoxyethyl or allyl, whereas, in the present invention, the corresponding group is methyl.

MedPointe further admits that the file history of the '644 application includes an Examiner's Action dated March 26, 1990 stating, *inter alia*:

The declaration supplied by the applicant, citing as unexpected the effectiveness of azelastine as compared with the preparation of Example 1 of Engel et al, is incomplete. The applicant claims several concentrations of azelastine in pharmaceutical preparations but does not indicate what concentration was used in the comparison studies.

To the extent that Counterclaim Paragraph 25 contains any other or different averments, MedPointe denies them.

#### **COUNTERCLAIM PARAGRAPH 26**

In response to the examiner's criticism of the declaration, the applicants filed a second declaration purporting to further describe the experimental method of the first experiment. However, that declaration did not describe the experiment conducted in the first declaration. Instead, it described a hypothetical experiment that involved application of azelastine directly to the nasal mucosa of research animals, an *in vivo* test. This test would have been more probative of the patentability of the application. However, the test that was actually conducted and described in the first declaration was an *in vitro* test that involved studying the effects of the drug on cells suspended in a buffered solution. The same declarant drafted both the first and second declarations and knew the second declaration did not describe the experiments actually conducted and could not be used to support patentability. The declarant was also an employee of Asta-Werke, but failed to disclose this fact to the PTO. The application later issued as U.S. Patent No. 5,164,194, the patent in dispute.

#### **REPLY TO COUNTERCLAIM PARAGRAPH 26**

MedPointe admits that the file history of the '644 application includes a declaration dated June 1, 1990 ("the June 1, 1990 Declaration") discussing the experiments described in the January 23, 1990 Declaration. MedPointe further admits that both the January 23, 1990 Declaration and the June 1, 1990 Declaration were signed by Istvan Szelenyi, then an employee of Asta Pharma. MedPointe further admits that the '644 application issued on November 17, 1992 as U.S. Patent No. 5,164,194. MedPointe further admits that the January 23, 1990 Declaration discussed experiments involving "sensitized rat peritoneal mast cells" in which



"[t]he mast cells are incubated first with a test substance and then challenged with antigen." MedPointe is without knowledge or information sufficient to form a belief as to the truth of the averments in the seventh sentence of Counterclaim Paragraph 26 and therefore denies them. To the extent that Counterclaim Paragraph 26 contains any other or different averments, MedPointe denies them.

#### **COUNTERCLAIM PARAGRAPH 27**

Helmut Hettche and Jurgen Engel participated in a scheme to materially misrepresent to the PTO the advantages and disadvantages of azelastine and derivative azelastine compounds in an effort to obtain a patent monopoly on azelastine medicines and derivative medicines. Jurgen Engel made knowingly false statements to the PTO in pursuing an application for azelastine derivatives. But for these statements, Jurgen Engel would not have been granted the '387 patent. Helmut Hettche later made knowingly false statements to the PTO in pursuing his application for azelastine containing medicines. But for these statements, Helmut [sic] Hettche would not have been granted the '194 patent application leading to the '387 patent application. [sic]

#### **REPLY TO COUNTERCLAIM PARAGRAPH 27**

Denied.

#### **COUNTERCLAIM PARAGRAPH 28**

Jurgen Engel was an employee at Asta-Werke while the applications leading to the '194 patent were filed and prosecuted. Helmut Hettche was also an employee of Asta-Werke and was a subordinate employee to Jurgen Engel at the time those applications were being filed. Helmut Hettche knew of the application leading to the '387 patent claiming derivative compounds to azelastine. Helmut Hettche participated in the development and testing of those compounds and was aware of the statements made in the application and prosecution. Jurgen Engel was also aware Hettche was developing the medicaments claimed in the '194 patent, including an aerosol of azelastine at the time he filed the application resulting in the '387 patent. In fact, both applications were prosecuted by the same U.S. law firm.

#### **REPLY TO COUNTERCLAIM PARAGRAPH 28**

Upon information and belief, MedPointe admits that the name and address of the law firm Cushman, Darby & Cushman appears in the prosecution histories of the '387 patent and

the '194 patent. MedPointe is without knowledge or information sufficient to form a belief as to the truth of the remaining averments of Counterclaim Paragraph 28, and therefore denies them.

**COUNTERCLAIM PARAGRAPH 29**

Helmut Hettche was aware that at least the compounds of Examples 2 and 4 of the '387 patent were almost 3 times more effective as antiallergy compounds than azelastine. Nonetheless, when prosecuting the application that resulted in the '194 patent, Hettche represented to the PTO that azelastine was twice as effective as the compound of Example 1 of the '387 patent. Although Helmut Hettche knew the compounds of Examples 2 and 4 of the '387 patent were nearly three times as effective as azelastine, Hettche intentionally failed to disclose this fact to the PTO. The applicant knew that if he demonstrated the superior properties of the '387 compounds that he would not be able to overcome a prima facie finding of obviousness by the examiner.

**REPLY TO COUNTERCLAIM PARAGRAPH 29**

Denied.

**COUNTERCLAIM PARAGRAPH 30**

Helmut Hettche was also aware that Jurgen Engel had previously disclosed the superiority of the '387 patent compounds to the PTO. In an effort to further argue azelastine was superior to the compounds disclosed in the '387 patent and to throw the Examiner off track, the applicant misrepresented study protocols and results described in the first declaration filed in support of the application. These misrepresentations were designed to make the method of application of azelastine claimed in the '194 patent application appear superior to application of the compounds disclosed in the '387 patent administered in the same manner. In fact, Hettche never presented results of these types of comparison studies.

**REPLY TO COUNTERCLAIM PARAGRAPH 30**

Denied.



**COUNTERCLAIM PARAGRAPH 31**

Helmut Hettche also misrepresented the state of the prior art in seeking to overcome the examiner's rejection of the Hettche application as anticipated by the '384 prior art patent. In the paragraph bridging columns 6 and 7 of that patent, the '384 prior art patent discloses administering azelastine "in the usual embodiments such as tablets, dragees, capsules, suppositories, drops, ointments, creams as well as injection solutions." The applicants of the '194 patent argued that this reference as interpreted by a person skilled in the art does not disclose that drops are administered to the patient. However, the applicants knew that Jurgen Engel had already argued to the PTO that the ability to administer antiallergic compounds as aerosols were [sic] important for the treatment of conditions described in the '194 patent application. It is well known in the art that aerosols are a form of administering drops. In fact, the '194 patent application admits drops are routinely administered to patients to treat allergies wherein at column 2, lines 12 through 17 the applicant states the preferred methods of administering azelastine are in the forms of "drops, ointments, [and] creams ..." These were the exact modes of administering azelastine as disclosed in the '384 patent. Nonetheless, the applicants for the '194 patent continued to attempt to confuse and confound the examiner by arguing that one skilled in the art would not have understood the drops of azelastine disclosed in the '384 patent to be administered directly to the patient.

**REPLY TO COUNTERCLAIM PARAGRAPH 31**

MedPointe admits that U.S. Patent No. 3,813,384 ("the '384 patent") states:

The compounds according to the present invention are used as active ingredients in pharmaceutical preparations and may be administered in usual embodiments such as tablets, dragees, capsules, suppositories, drops, ointments, creams as well as injection solutions.

(U.S. Patent No. 3,813,384, col. 6, ll. 66-70.) MedPointe further admits that the '194 patent states:

The preferred embodiment of the invention is a sterile and stable aqueous solution of azelastine or one or more of its salts which can be used in the form of drops, ointments, creams, gels, insufflatable powders or, in a particularly preferred embodiment, in the form of a spray (preferably a nasal spray).

(U.S. Patent No. 5,164,194 , col. 2, ll. 12-17.) To the extent that Counterclaim Paragraph 31 contains any other or different averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 32**

A reasonable opportunity for further investigation or discovery is likely to provide evidentiary support that the foregoing misrepresentations and failure to disclose material prior art as set forth above were done with intent to mislead the PTO.

**REPLY TO COUNTERCLAIM PARAGRAPH 32**

Denied.

**COUNTERCLAIM PARAGRAPH 33**

The facts and circumstances set forth in this Count IV constitute inequitable conduct on the part of the applicants, making the '194 patent unenforceable.

**REPLY TO COUNTERCLAIM PARAGRAPH 33**

Denied.

**COUNTERCLAIM PARAGRAPH 34**

A reasonable opportunity for further investigation or discovery is likely to provide evidentiary support for other and further circumstances constituting inequitable conduct by the applicants.

**REPLY TO COUNTERCLAIM PARAGRAPH 34**

Denied.

**COUNTERCLAIM PARAGRAPH 35**

Apotex Inc. and Apotex Corp. repeat, reallege and incorporate by reference each of the allegations of paragraphs 1 through 34 as though set forth fully herein.

**REPLY TO COUNTERCLAIM PARAGRAPH 35**

MedPointe restates its responses to Counterclaim Paragraphs 1 through 34 as though fully set forth herein. To the extent that Counterclaim Paragraph 35 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 36**

Neither Apotex Inc. nor Apotex Corp. infringes, either directly or indirectly, any valid claim of the '194 patent. ANDA 78-621 does not infringe, either directly or indirectly, any valid claim of the '194 patent. The proposed drug product for which approval is sought under ANDA 78-621 does not directly or indirectly infringe any valid claim of the '194 patent.

**REPLY TO COUNTERCLAIM PARAGRAPH 36**

Denied.

**COUNTERCLAIM DEMAND FOR JUDGEMENT AND PRAYER FOR RELIEF**

WHEREFORE, Apotex Inc. and Apotex Corp. pray for judgment:

- a. Finding that the '194 patent is invalid and unenforceable;
- b. Finding that the '194 patent is not infringed in any manner by either Apotex Inc. or Apotex Corp.;
- c. Finding that this is an exceptional case under 35 U.S.C. § 285;
- d. Awarding to Apotex Inc. and Apotex Corp. their costs, expenses, and reasonable attorney's fees and other relief the Court deems just.

**REPLY TO COUNTERCLAIM DEMAND FOR JUDGEMENT  
AND PRAYER FOR RELIEF**

MedPointe denies that Apotex is entitled to any relief whatsoever from MedPointe or the Court, either as prayed for in its Counterclaims or otherwise.

MedPointe further denies each and every allegation contained in Apotex's Answer, Defenses, and Counterclaims that was not specifically admitted, denied or otherwise responded to in this Reply.

**COUNTERCLAIM DEMAND FOR JURY TRIAL**

Apotex Inc. and Apotex Corp. demand trial by jury for all issues triable by jury. This demand is contingent upon MedPointe seeking monetary damages as set forth in paragraph D of its prayer for relief in its complaint.

**REPLY TO DEMAND FOR JURY TRIAL**

MedPointe denies that Apotex is entitled to a jury trial. MedPointe further denies that there are any issues in this action that are triable by jury.

**MEDPOINTE'S PRAYER FOR RELIEF**

**WHEREFORE**, MedPointe prays for judgment as follows:

- A. Dismissing Apotex's Counterclaims with prejudice;
- B. Awarding MedPointe the relief sought in its Complaint;
- C. Awarding MedPointe its costs, attorneys' fees and expenses incurred in this action; and
- D. Awarding MedPointe such further relief as the Court deems just and proper.

*Of Counsel:*

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Dated: June 19, 2007



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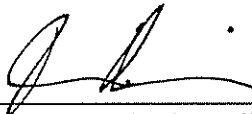
**CERTIFICATE OF SERVICE**

I HEREBY CERTIFY that on June 19, 2007, I electronically filed the foregoing document with the Clerk of Court using CM/ECF which will send notification of such filing, and hand delivered to the following:

Richard L. Horwitz, Esq.  
POTTER ANDERSON & CORROON LLP  
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I HEREBY CERTIFY that on June 19, 2007, I sent the foregoing document by Federal Express, next business day delivery, to the following non-registered participant:

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